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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/664,456 | 09/19/2003 | Douglas P. Cerretti | 2517-USB | 5621 |

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| EXAMINER | |
|---|---|
| MOORE, WILLIAM W | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1656 | |

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/664,456 | CERRETTI, DOUGLAS P. | |
| | Examiner | Art Unit | |
| | William W. Moore | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *12,13,24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,14-23 and 26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20030919*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Preliminary Amendment and Specification*

Applicant's Preliminary Amendment filed with the application on 19 September 2003 has been entered, revising information at page 1, line 9, of the specification, deleting the terms "http" and associated punctuation at pages 33, 34, and 47 of the specification, and providing the new claims 1-31.

The disclosure is objected to because of the following informalities: It is noted that the amendment to page 1 of the specification does not indicate the status of the parent application serial No. 09/890,323, which is now abandoned. Applicant is invited to amend the specification to indicate the status of the parent application in response to this communication. While several instances of signals for embedded hyperlinks were altered in Applicant's Preliminary Amendment, the disclosure is objected to because it still contains embedded hyperlinks and/or other form of browser-executable code. See page 4 at lines 12-14. Applicant is required to delete all instances of embedded hyperlinks and/or other form of browser-executable code wherever they occur in the specification. See MPEP § 608.01. Appropriate correction is required.

### *Election/Restrictions*

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

1. Claims 1-11, 14-23, and 26-31, drawn to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:12, classified in class 435, subclass 219.
2. Claims 1-10, 12, 14-22, 24, and 26-31, drawn to an isolated polypeptide that comprises the amino acid sequence of SEQ ID NO:13, classified in class 435, subclass 219.
3. Claims 1-10, 13-22, and 25-31, drawn to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:14, classified in class 435, subclass 219.

Inventions of Groups 1, 2 and 3 are unrelated, each to the other, because each comprises a distinct product having a unique primary structure. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed

to be used together and require separate searches in the patent and non-patent literature.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Ms. Susan Lingenfelter on 10 June 2005 a provisional election was made with traverse to prosecute the invention of Group I, comprising claims 1-11, 14-23, and 26-31, drawn to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:12. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12, 13, 24 and 25 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1-10, 14-22, and 26-31 are objected to because they are drawn, in part, to non-elected subject matter.

*Claim Rejections - 35 USC § 101*

35 U.S.C. §101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-11, 14-23, and 26-31 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility.

A claimed invention must posses a specific, substantial and credible *in vitro* or *in vivo* utility. It is agreed that SEQ ID NO:12 encodes a metalloprotease comprising a protease domain and a disintegrin domain and that both domains share detectable degrees of amino acid sequence identity with protease and disintegrin domains in the prior art. The specification, however, discloses no specific *in vitro* or *in vivo* utility for either the disintegrin domain or the protease domain of the SVPH-1a amino acid sequence set forth in SEQ ID NO:12. The specification teaches that mRNA transcripts encoding the SVPH-1a metalloprotease can be detected in human testicular tissue and, at page 1, that disintegrin domains generically are known to bind to integrins, molecules expressed on the surface of cells, "involved in cell-to-cell adhesion, cell-to-matrix

adhesion, and inflammatory responses". The specification also teaches, at page 3, that disintegrin domains of proteins in snake venom "prevent[ ] platelet aggregation and . . . act[ ] as an anticoagulant", and further teaches, page 5, that that the SVPH-1a metalloprotease may be used to study "cell/cell and cell/matrix interactions involved in cellular processes . . . as well as those [processes] involved in the immune system". In addition to these teachings generic to disintegrin domains, the specification proposes utilities generic to proteins as a whole, e.g., in the final paragraph of page 38, that the SVPH-1a polypeptide may be used as a "research tool for studying the biological effects that result from inhibiting binding . . . interactions on different cell types" and, at pages 39-43 that either the protease or the disintegrin domain might be used as molecular weight markers and as controls for peptide fragmentation.

But the specification is silent about the nature of any cellular process that requires the presence or activity of the integral SVPH-1a metalloprotease or the 103-amino acid disintegrin domain required by claims 1-5, or the closely-related metalloproteases and disintegrin domains defined by the hybrization conditions or the requirement for 95% identity stated in claims 6-11, 14-23, 26 and 28-31. The specification cannot identify the nature of the activity of the protease domain, whether exoproteolytic or endoproteolytic, whether it acts within a cell or acts outside a cell, and also fails to identify the nature of any substrate for protease domain. Similarly, the specification is silent as to the nature of any specific cell/cell or cell/matrix interaction that might be affected by the disintegrin domain within SEQ ID NO:12. The assertion that a claimed product may be used as a molecular mass marker does not rise to the level of a specific utility - other polypeptides will serve this purpose - and no disclosure in the specification indicates that at the time the application was filed Applicant was aware of any specific utility for a SVPH-1a metalloprotease or its included disintegrin domain, that would permit its immediate use by the public. A method of using a material for further research to determine, e.g., its

specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966).

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 14-23, and 26-31 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1, 3-10, 14-22 and 26-31 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification fails to exemplify or describe the preparation of a polypeptide that comprises the divergent amino acid sequences of claims 1, 3-10, 14-22, and 26-31 that may differ from the amino acid sequence set forth in SEQ ID NO:12 beyond the region identified in claim 1, where the limitation "having disintegrin activity" is unsupported by the specification where the nature of the activity is undisclosed and is not demonstrated to reside entirely in the amino acid sequence region identified in claim 1. In particular, claim 27 reaches generic peptides or polypeptides that differ at as many as 10 amino acid positions within the 103-amino acid sequence of the region identified in claim 1 as well throughout the rest of the molecule. Neither the claims nor the specification can describe where amino acid differences may occur within SEQ ID NO:12 that confer the undisclosed activity nor what the differences might be. "While one does not need to have carried out one's invention before filing a patent application, one does need to be

able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of polypeptides that differ from the amino acid sequence of SEQ ID NO:12 yet have "disintegrin activity", thus the specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structure of the claimed molecules.

Claims 1, 3-10, 14-22, and 26-31 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the preparation of a polypeptide having the amino acid sequence of the elected SEQ ID NO:12 having a disintegrin activity, does not reasonably enable preparation of amino acid sequences having disintegrin activity that diverge from the amino acid sequence of SEQ ID NO:12 by unlimited amino acid substitutions, deletions and insertions, or combinations thereof anywhere within SEQ ID NO:12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3-10, 14-22 and 26-31 are rejected for lack of enablement because they embrace unlimited, arbitrary, amino acid substitutions, additions or deletions anywhere, in any combination or pattern, within SEQ ID NO:12 but he specification cannot support such insertions, deletions, or substitutions anywhere the SVPH-1a amino acid sequence SEQ ID NO:12 yet assure a product that retains an undisclosed disintegrin activity where neither the specification nor the prior art made of record, taken together, teach where any amino acid positions might be altered, nor the nature of the alterations that may be made, which permit a resulting variant amino acid sequence to have "disintegrin activity". The specification teaches no specific disintegrin activity for the native SVPH-1a disintegrin domain of SEQ ID NO:12 with which the artisan, seeking to make even a few alterations, might assay to determine whether or not an alteration of SEQ ID NO:12 results in the loss or the retention of disintegrin activity and mere sequence perturbation will not enable the design and preparation of divergent disintegrin domains that might provide the public domain that retains its undisclosed, native, function.

It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Applying the analysis of enablement discussed in *Wands* to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the SVPH-1a amino acid sequence of SEQ ID NO:12 to the extent permitted by the claims,

b) the specification lacks working examples wherein the SVPH-1a amino acid sequence of SEQ ID NO:12 is altered to the extent recited in the claims,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no members of the class of proteases represented by the amino acid sequence of SEQ ID NO:12 had even a few amino acid positions identified for concurrent modification.

Thus the scope of subject matters embraced by amino acid sequence alterations beyond the region identified in claim 1, and particularly amino acid sequence alterations embraced by claim 27 within the region identified in claim 1, is unsupported by the present specification, even if combined with the teachings available in the prior art.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11, 14-23, and 26-31 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 6, 15 and 27 are indefinite in stating, "having disintegrin activity", where the nature of the recited activity is not disclosed in the specification, thus the artisan and the public seeking to determine the metes and bounds of the intended subject matter cannot know what is covered by the claims. Claims 2-5, 7-11, 14, 16-23, 26, and 28-31 are included in this rejection because they depend from claims 1, 6, 15 and 27 but do not otherwise resolve the ambiguity of the claims from which they depend.

*Conclusion*

While rejected above under 35 U.S.C. §§ 101 and 112, claims 1-11, 14-23, and 26-31 describing either the integral SVPH-1a metalloprotease of SEQ ID NO:12 or a polypeptide that comprises the included disintegrin domain comprising amino acids 389 through 491 of SEQ ID NO:12 are free of the prior art of record herein, including the prior art made of record with Applicant's Information Disclosure Statement filed 19 September 2003. The ADAM 20 metalloprotease-disintegrin disclosed in 1998 by Hooft van Huijsduinen has an amino acid sequence that shares an overall 48.7% identity with that of SEQ ID NO:12 herein and shares 72.5% identity in the region corresponding to the disintegrin domain described by claim 1. There is no disclosure before Applicant's January 1999 priority date of a disintegrin domain amino acid sequence having a closer sequence relationship to the disintegrin domain of SEQ ID NO:12 herein than that of ADAM 20 metalloprotease-disintegrin.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Ponnathapura Achutamurthy, can be reached at 571.272.0928. The fax phone number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
25 June 2005

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER